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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,377	02/12/2001	Andre Rosenthal	147-211P	7286

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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/647,377	Rosenthal et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *March 10 and April 28, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above, claim(s) *9-11, 14-19, 22, 27, 28, and 30-35* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 12, 13, 20, 21, 23-26, 29, and 36-41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Apr 28, 2003* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendments filed 3/10/03 and 4/28/03 have been entered. Claims 1, 2, 4, 7, 8, 12 and 13 have been amended. Claims 29-41 have been added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

Claims 9-11, 14-19, 22, 27 and 28 in their entirety and claims 1-8, 12, 13, 20, 21, and 23-26 as directed to SEQ ID NOs 13 and 14 remain, and new claims 30-35 in their entirety and new claims 37-41 as directed to SEQ ID NOs 13 and 14, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12. The requirement was made FINAL in the Office action of 9/3/02.

New claims 30-35 are directed to the nonelected inventions of groups III-VIII. New claims 37-41 are directed in part to the nonelected invention of group II. Applicant has provided additional arguments in traversal of the restriction requirement between groups I and II. It is inappropriate to direct such arguments directed to the examiner after the restriction has been made FINAL. Consequently, the arguments have not been considered. Applicant may, if desired, direct such arguments to the Director of Technology Center 1600 in a petition under 37 CFR 1.144.

This application contains claims 9-11, 14-19, 22, 27, 28 and 30-35, entirely, and claims 1-8, 12, 13, 20, 21, 23-26, and 37-41, in part, drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

The corrected or substitute drawings were received on 3/10/03 (or 4/28/03). These drawings are not acceptable for the reasons set forth on the attached PTO-948 and the conditions for accepting color photographs have not been met. Specifically, the papers filed 4/28/03 lack a petition under 37 CFR 1.84(a)(2) and three sets of color drawings or color photographs, as appropriate. No petition was attached to the papers, only one set of color photographs was present. Color photographs will be accepted if the conditions for accepting color drawings have been satisfied. With respect to Figures 1 and 8 filed 4/28/03, the color photographs have or are falling off of the sheet. Figures 1 and 8 as filed 3/10/03 would be acceptable.

Specification

This application contains sequence disclosures in Figure 2a-2m that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825. Most of the amino acid sequences disclosed in Figure 2a-2m have not been

included in the Sequence Listing as required under 37 C.F.R. §§ 1.821 (c) & (e). Also, neither the "Brief Description" of the figure (preferred) or the figure itself must identify the sequences by their assigned SEQ ID NOs, 37 C.F.R. §§ 1.821 (d).

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action which fails to meet *all* of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 101 & 112

Claims 1-7, 20, 21, 23-26 remain rejected and claims 8, 12, 13, 29, and 36-41 are rejected under 35 U.S.C. 101 for the reasons of record set forth in the Office action of 9/3/02, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Also, claims 1-7, 20, 21, 23-26 remain rejected and claims 8, 12, 13, 29, and 36-41 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 3/10/03 have been fully considered but they are not persuasive. Applicant asserts the specification discloses at page 7 that "LOBO proteins are involved in mitosis and cell cycle, as well as, human growth disorders not caused by nutrition or hormones." However, page 7 simply postulates biological functions for LOBO, and states that the "nucleic acid molecules of the invention *could be* responsible for human growth disorders not caused by nutrition or hormones" (emphasis added). It does not unequivocally assert that LOBO possesses any of these functions. More importantly, it does not describe a use for the claimed invention other than as an object of scientific inquiry, i.e. page 7 does nothing more than present likely avenues for further research on the claimed invention.

Applicant asserts that page 1 "identifies several growth diseases that may be treated with using the present invention." However, page 1 (paragraph 2) simply mentions that hereditary diseases resulting in impaired growth and development exist in humans and that their genetic causes are unknown and that early diagnostic methods and therapeutic treatments are unavailable. Nowhere does page 1 identify a hereditary disease that can either be diagnosed or treated using the claimed invention, and it clearly does not indicate that achondroplasia can be treated.

Applicant asserts that one of ordinary skill in the art would realize that reducing the expression of the LOBO gene would ameliorate achondroplasia. Firstly, no evidence has been provided that one of ordinary skill in the art "would immediately realize" that reducing expression of LOBO would ameliorate achondroplasia. More importantly the specification fails

to teach such a use. Secondly, Example 7 discloses that loss of function of human LOBO may be responsible for AHO, characterized by hyposomia (short bones). If true, reducing LOBO expression in achondroplasia would either do nothing or would exacerbate the condition. Thirdly, the claims are not directed to a compound that would reduce expression of LOBO, but to nucleic acids that would encode, and presumably increase LOBO expression.

Applicant also asserts that based on the disclosures of Fig. 4 and Example 1 one of skill in the art would know that the LOBO gene may be used for cartilage tissue engineering and for producing cartilage or tissue substitutes. Applicant provides no explanation as to how one of skill would arrive such at such a use, particularly since the specification makes no mention of such a use and Example 1 describes the construction and phenotype of a mouse which lacks LOBO, not one to which a LOBO gene was added.

Both of these "uses" are highly speculative and unsupported either in the specification or by any extrinsic evidence provided by Applicant. At issue here is what specific and substantial uses for the claimed invention the specification teaches, not whether one of skill may be able in the future to identify such uses. Whether or not the claimed invention may in the future be found to have undisclosed uses is not dispositive of the instant rejection. See *In re Kirk*, 153 USPQ 48 (CCPA 1967), particularly at pages 52-53.

Applicant notes that Example 7 discusses the "connection between LOBO protein and AHO." The relevance of this statement is unclear, especially since Example 7 points out that the

consequences of loss of function of LOBO in mice and loss of function of the AHO gene in humans are nearly opposite (megasomia in mice vs. hyposomia in humans), and points out that humans and mice are quite different in many respects. In other words, if the AHO gene is the human ortholog of murine LOBO, it would appear that their biological functions are not the same.

The reference to page 14 is unclear, page 14 has two complete and two partial paragraphs. The first complete paragraph generally discusses only the preparation and delivery of pharmaceutical compositions, and does not discuss any patients to be treated. The second full paragraph discusses making transgenic non-human animals as disease models.

Claims 1-7, 20, 21, 23-26 remain rejected and claims 8, 12, 13, 29, and 36-41 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 9/3/02, and the additional reason set forth below for claim 40 , as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitations directed to nucleic acid molecules encoding protein that is at least a certain percentage identical to SEQ ID NO: 9 has no impact on the original grounds of rejection. The claims are still limited to nucleic acids encoding natural proteins which deviate in amino acid sequence from SEQ ID NO: 9, and whose specific structures have not been disclosed or

described in such a way that would distinguish them from other structurally similar proteins not embraced by the claims. Inclusion of the percent identity limitations does not provide any information that would allow one to envision other members of the claimed genus.

New claim 40 recites the limitation "homology of at least 97% to ...". Applicant has not indicated where or how the original specification supports this limitation, as is Applicant's burden. MPEP 714.02, last sentence of third para. from end, & MPEP 2163.06(I), last sentence. Page 9, first full para., of the specification supports the limitation to homology of at least 70%, 80%, 90% or 95%, but there is no indication that the genus of claim 40 was contemplated.

Applicant's arguments filed 3/10/03 have been fully considered but they are not persuasive. Applicant argues that pages 7-10 provides support for a generic nucleic acid whose complement hybridizes to a murein LOBO nucleic acid and which meets the phenotypic limitation. However, all pages 7-10 describe is hybridization conditions and the use of disclosed sequences as probes and sequence identity between variants and the disclosed sequences. Such variants are not restricted to those being claimed which encode natural LOBO proteins whose loss or reduction results in elongated bones. Applicant is again reminded that the courts and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of

the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. The recited structural limitations, i.e. hybridization or percent homology, do not inform one of the detailed constitution of the nucleic acids embraced by the claim. At best, the disclosure implies how one might go about isolating such nucleic acids. The various structurally related proteins discussed on pages 6-7 do not inform one of what structural features are possessed by the proteins embraced by the claims that distinguish them from those which are structurally related but clearly have different biological functions.

With respect to human vs. murine LOBO, the Office accepts that Applicant cannot be expected to test whether knocking out the human LOBO gene would produce a phenotype similar to knocking out murine LOBO. However, the specification in Example 7 identifies a potentially

naturally occurring knock-out mutation in human LOBO that results in AHO. If true, the consequences of loss or reduction of LOBO function in humans results in a quite different phenotype than was observed in mice, i.e. nucleic acid molecules encoding human LOBO protein would NOT meet the phenotypic limitation of the claim.

Applicant asserts that the specification would lead one of skill in the art to conclude that inactivation or reduction of human LOBO could be used to treat AHO (or symptoms of AHO). The basis for this statement is not explained, particularly since Example 7 makes no such claim. Furthermore, Example 7 clearly indicates that AHO results from loss of gene function, possibly loss of LOBO gene function. Consequently, further reducing LOBO expression would simply make AHO symptoms more severe (in cases where AHO gene function is reduced but not completely lacking). The disparity in phenotype between mice lacking LOBO function and human AHO patients was noted in Example 7, and the specification discusses how such disparity may not necessarily preclude the human LOBO gene as being the AHO gene. The last sentence in Example 7 notes that mutation of the same (i.e. orthologous) gene in mouse and human "can lead to quite different phenotypes, because these organisms are different in many respects."

The relevance of Applicant's comments on the structural relationship between human and murine LOBO protein and nucleic acids is unclear. Applicant has provided no evidence that this structural relationship means that the human and murine LOBO share the same function. If the AHO gene in humans is the LOBO gene, then clearly they do not share the same physiological or developmental function in these organisms as a whole. At best, this structural relationship

implies similar biochemical activity or physiological activity at the cellular level. However, this biochemical activity no longer serves the same role in these two organisms which "are different in many respects." The claims do not recite a biochemical activity nor does the specification disclose a biochemical activity for LOBO. It merely postulates potential biochemical activities, e.g. binding to an unidentified RNA or G protein (page 7).

It is also unclear how the absence of proteins with at least 70% identity to murine LOBO in the prior art supports claims to corresponding nucleic acids which the instant specification also fails to disclose, other than nucleic acids which encode SEQ ID NO: 9. The fact that no one else possessed a nucleic acid readable on the claims simply means that the claims comply with 35 USC 102 or 103.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 29 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Claims 8 and 29 are directed to a method for preparing a protein encoded by the nucleic acid molecule of claim 1. However, the method step which follows fails to recite any element possessed by the recited "host cell" which would lead to expression of such a protein, e.g. a nucleic acid molecule of claim 1 comprising regulatory elements which ensure the expression of the protein encoded by the nucleic acid molecule.

Claim Rejections - 35 USC § 102

Claim 7 remains rejected under 35 U.S.C. 102(b) as being anticipated by Browning et al. (Proc. Natl. Acad. Sci. USA 94: 14637-14641, 1997) for the reasons of record set forth in the Office action of 9/3/02.

The amendment to claim 7 does not address the grounds of rejection, which were already directed to transformed cells.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are

also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

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